

Panel Discussion #3:

Challenges in the Implementation of ePROs in clinical trials

*FOURTH ANNUAL
PATIENT-REPORTED OUTCOME (PRO) CONSORTIUM WORKSHOP*

April 24, 2013 ■ Silver Spring, MD

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- Why an ePRO?
- Collaborative efforts between PRO Consortium and ePRO Consortium
- Challenges in the implementation of ePROs in clinical trials
 - Pharmaceutical Industry Perspective
 - ePRO Vendor Perspective
- Q and A

Why ePRO?

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The emergence of technologies that enable the direct electronic capture of patient-reported data has been one of the most important developments in the field of PRO assessment.

Based on evidence that has been mounting over the past 20 years, paper-based self-reports of measurements (e.g., peak flow values) and experiences or sensations (e.g., symptoms) are far from optimal compared with data collected electronically.^{1,2}

As stated by Ganser and colleagues,³ paper-based approaches to patient-reported data collection can result in

- **untimely**
- **unreadable**
- **missing**
- **illogical or otherwise faulty data**

“If a patient diary or some other form of unsupervised data entry is used, we plan to review the clinical trial protocol to determine what steps are taken to ensure that patients make entries according to the clinical trial design and not, for example, just before a clinic visit when their reports will be collected.”⁴ (pg 14)

The transition from paper diaries and questionnaires to electronic (ePRO) systems for PRO data collection has enhanced the integrity and accuracy of data collected in clinical trials.³

This transition, along with the FDA's PRO Guidance, has elevated the science of PRO measurement.

Electronic data collection systems can provide^{2,5-12}

- more accurate and complete data
- avoidance of secondary data entry errors
- easier implementation of skip patterns
- less administrative burden
- potential cost savings

...is essential due to the significant role PRO endpoints play.

As evidence of this significance,

Gnanasakthy et al. found that of the 116 NMEs and BLAs approved by the FDA from 2006 through 2010, 28 (24%) were granted PRO-based label claims.¹³

Of those 28 products, 20 (71%) used a PRO as a primary clinical trial efficacy endpoint.

**Two more recent FDA approvals,
Incyte's Jakafi (ruxolitinib) and
Insys Therapeutics's Subsys (fentanyl SL spray),
have PRO-based label claims supported by data
collected on ePRO systems (i.e., eDiaries).¹²**

ePRO-based data collection can enhance the integrity and accuracy of data collected in clinical trials.

However, deployment of an ePRO system in a clinical trial requires a partnership between the sponsor's clinical trial team and the ePRO system provider.

A collaborative approach with open, effective lines of communication is essential to avoid the avoidable and quickly resolve any challenges that emerge.

Clinical trial sponsors and ePRO providers share a common goal – obtaining high quality PRO data.

This session is intended to foster the type of constructive dialog necessary to fulfill this goal.

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Collaborative Efforts between PRO Consortium and ePRO Consortium

**Sonya L. Eremenco, MA and Cindy Howry, MS –
Bracket, a subsidiary of United BioSource
Corporation**

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Collaborative efforts between PRO Consortium and ePRO Consortium



- Structure:
 - Coordinating Committee
 - Instrument Migration Subcommittee
 - Subcommittee for Research
 - Subcommittee for Publications and Presentations
- ePRO Collaboration between ePRO Consortium and PRO Consortium ePRO Subcommittee
 - Deviation from ePRO Plan
 - Opt-Out

- Develop principles of good practice
 - Principles for Migration of Existing Instruments
 - Principles for New Instrument Development
 - Best Practices for the Electronic Implementation of COA Response Sets
- Available on the ePRO Consortium Web Site under Resources at:
 - <http://www.c-path.org/ePRO.cfm>

- Conduct Electronic Implementation Assessments of new PRO Consortium instruments in development
 - Depression
 - IBS
 - Asthma
- Develop ePRO technology-cognitive interview phase of content validity stage
- Develop ePRO technology-quantitative study phase of content validity stage

Electronic Implementation of IBS-C, IBS-D, and IBS-M



- Electronic implementation of new IBS instruments
- General Considerations (from Principles for Migration of Existing Instruments)
 - Context of use – relevant patient population
 - Instrument characteristics – format (underline, boldface), length of questionnaire and/or items
 - Regional considerations – Internet connectivity, translated text
 - Electronic considerations – potential benefits, level of change

Electronic Implementation Assessment for IBS WG Instrument



- To date:
 - Conducted an Electronic Implementation Assessment
 - Performed an item-level analysis of the IBS instrument's for electronic implementation on IVR, handheld, tablet and web
 - Provided screen mock-ups of IBS WG Instrument for handheld
 - Finalizing screen layout, branching, recall period and other electronic functionality.


Challenges and Considerations

- Length of responses and number of responses
- Display entire question and items/responses on one screen with no scrolling








3. Please describe the form of your stool using the following scale where:




- 1=Separate hard lumps like nuts (difficult to pass)
- 2=Like a sausage but lumpy
- 3=Like a sausage but with cracks on the surface
- 4=Like a sausage or snake, smooth and soft
- 5=Soft pieces with clear-cut edges (easy to pass)
- 6=Fluffy pieces with ragged edges, a mushy stool
- 7=Watery, no solid pieces (entirely liquid)

[Note: Item 3 (BSFS) will be administered with pictures.]

Please describe the form of your stool using the following scale where: 

Type:

1	Separate hard lumps like nuts (difficult to pass)	
2	Like a sausage but lumpy	
3	Like a sausage but with cracks on the surface	
4	Like a sausage or snake, smooth and soft	
5	Soft pieces with clear-cut edges (easy to pass)	
6	Fluffy pieces with ragged edges, a mushy stool	
7	Watery, no solid pieces (entirely liquid)	

 Back  Exit  Next

Challenges and Considerations



- Recall period and entry of past events
- Minimum font size for handheld
- Minimum screen size for electronic implementation
- Minimum required edit checks for electronic implementation

- Complete ePRO technology-cognitive interview phase of content validity stage
 - Finalize requirements document with mock screens including parameters for implementation
 - Perform cognitive interviews
 - Revisions to the IBS instrument based on cognitive interviews
- Develop ePRO technology-quantitative study phase of content validity stage

Challenges in ePRO Planning and Implementation

Industry and ePRO Vendor
Perspectives



Panel Members



Industry Panel	ePRO Vendor Panel
Heather Blaudow, Eli Lilly & Company	Tim Davis, Exco Intouch
Sarah Fleming, Janssen Pharmaceutical	Cindy Howry, Bracket
Alison Greene, Roche-Genentech	Willie Muehlhausen, ICON
Tara Symonds, Pfizer	Paul O'Donohoe, CRF Health
	Jean Paty, ERT
	Sheila Rocchio, PHT
	Eric Ross, Almac

Moderator: Risa Hayes, Eli Lilly & Company

- RFP/Proposal
- Preparation
- Study Launch
- Execution
- Close-Out

- Internal alignment
- Protocol details
- Timelines and budget
- Roles and responsibilities

- Internal team – required expertise
- Realistic expectations/assumptions
- Logistical issues
- Sponsor testing of ePRO

- Technical v. “protocol flow” training
- Site-based v. take-home training
- Tools for ePRO success
 - Compliance reports
 - Training & Help materials
 - Time challenges

- Roles and responsibilities
- Risk mitigation (contingency plan)
- Compliance
- Reports

- Lessons Learned
- Getting the right data to the right people at the right time

- Plan early
- Ensure right people involved at right time
- Train the trainer
- Plan for deviations
- Learn from mistakes

Questions?